REMARKS

Status of the Claims

Claims 33 and 53-82 are currently pending. Claim 1-32 and 34-52 are canceled without prejudice or disclaimer of the subject matter claimed therein. Claims 33, 53-57, 61, 62, 64, 66, 68, 70-73, and 78 are withdrawn from consideration as being directed to a non-elected subject matter. Claims 58-60, 63, 65, 67, 69, 74-77, and 79-82 are under examination.

The Office Action indicated that claims 59, 74, 76, and 82 are withdrawn from consideration as being directed to a non-elected subject matter. However, claims 59, 74, 76, and 82 read on the elected species "particles" as the cationic component. Accordingly, claims 59, 74, 76, and 82 are directed to the elected subject matter and should be examined with claims 58, 60, 63, 65, 67, 69, 75, 77, and 79-81.

Rejection Under 102(b)

Claims 58, 60, 63, 65, 67, and 69 are rejected under 35 U.S.C. 102(b) as being anticipated by WO 96/04017A1 (Kresse, English Equivalent U.S. Patent 6,048,515).

The Office Action alleges that Kress discloses nanoparticles containing an iron-containing core, a primary coat of synthetic polymer, and a secondary coat of target polymer, and optional auxiliary pharmaceutical substances. However, Kresse does not teach targeting an activated vascular site and does not disclose a specific range of zeta potential or a specific isoelectric point that is effective for targeting an activated vascular site. Hence, Kresse does not disclose a method of modifying an agent comprising associating the agent with one or more cationic components to produce a composition having a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCl solution at about pH 7.5 for targeting an activated vascular site or a composition comprising molecules having an isoelectric point above 7.5. Kresse does not teach obtaining compositions having specific zeta potential range or specific isoelectric point for targeting activated vascular site. Moreover, Kresse does not teach selecting nanoparticle compositions having an optimal zeta potential for targeting an activated vascular site. Further, Kresse does not disclose enhancing the efficacy of targeting an activated vascular site by associating the nanoparticles with a cationic component to produce a composition with an

optimal zeta potential. Kresse does not teach increasing the efficacy of targeting to an activated vascular site by selecting for compositions having a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCl solution at about pH 7.5 or having an isoelectric point above 7.5. Kresse does not teach that a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCl solution at about pH 7.5 or an isoelectric point above 7.5 is associated with efficient targeting of the composition to an activated vascular site.

Also, Kresse discloses that negatively charged carriers in the nanoparticles are the preferred embodiments of the invention (see col. 12, line 7-9 and 34-37 and Examples B1-B4). Accordingly, Kresse teaches away from associating an agent with a positive/cationic component. Thus, the method of Kresse does not disclose the same method steps as the presently claimed method of modifying an agent to enhance its efficacy of targeting an activated vascular site.

The Office Action alleges that the compositions of Kresse inherently exhibit the same zeta potential, isoelectric point, and targeting properties as the compositions obtained by the methods of the present invention because they are made by the same method steps. However, Applicants respectfully point out that the claimed invention is a method of modifying an agent to enhance its efficacy. The claims are not directed to products. Moreover, as discussed above, the method of Kresse does not disclose the same method steps as the presently claimed invention. The method of Kresse does not require associating an agent with one or more cationic components to obtain a composition having a zeta potential of about +30 mV to +65 mV in about 0.05 mM KCl solution at about pH 7.5 or having an isoelectric point above 7.5. Therefore, Applicants respectfully submit that Kresse does not anticipate the claimed invention.

Rejection Under 35 U.S.C. § 103

Claims 75, 77, and 79-81 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/04017A1 (U.S. Patent 6,048,515, Kresse) as applied to claims 58, 60, 63, 65, 67, and 69 above, and further in view of Boehm *et al.* (Boehm).

The deficiencies of Kresse are discussed in detail immediately above. Boehm does not cure the deficiencies of Kresse. Boehm only discloses that zeta potential can improve the characterization of colloidal particles. Boehm neither discloses a zeta potential of about +30 mV to +65 mV, nor teaches any properties such as targeting which are associated with zeta potential.

Boehm neither discloses a method of modifying an agent to enhance its efficacy for targeting an activated vascular site nor teaches selecting a composition having a zeta potential in the range of about +30 mV to +65 mV in about 0.05 mM KCl solution at about pH 7.5 or having an isoelectric point above 7.5 for enhanced efficacy of targeting an agent to an activated vascular site. Accordingly, the cited references do not render the claimed invention obvious.

Conclusion

The foregoing amendments and remarks are being made to place the application in condition for allowance. Applicants respectfully request entry of the amendments, reconsideration, and the timely allowance of the pending claims. A favorable action is awaited. Should the Examiner find that an interview would be helpful to further prosecution of this application, she is invited to telephone the undersigned at her convenience.

If there are any additional fees due in connection with the filing of this response, please charge the fees to our Deposit Account No. 50-0310. If a fee is required for an extension of time under 37 C.F.R. §1.136 not accounted for above, such an extension is requested and the fee should also be charged to our Deposit Account.

Respectfully submitted,
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